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PSEUDODIPHThERIA BACILLI AS THE CAUSE OF SUPPURATIVE OTITIS, ESPECIALLY THE POSTSCARLATINAL.*

ALICE HAMILTON.

(From the Memorial Institute for Infectious Diseases, Chicago.)

THE pseudodiphtheria bacillus has been a subject of dispute, of contradictory opinions, since it was first described; but upon one point there has been almost complete harmony. Whatever disagreement there may have been as to its morphology, its cultural and chemical properties, or its relation to the diphtheria bacillus, there has been a striking unanimity as to its unimportance.¹ Although it is often found in inflammatory processes, either alone or together with other organisms, still it is usually regarded as a harmless saprophyte, an accidental accompaniment of the pyogenic organisms which are really doing the work. Another view, not essentially different, is that this bacillus is only a non-virulent variety of the Klebs-Löffler bacillus.

The reasons for relegating the pseudodiphtheria bacillus to the rank of non-pathogenic organisms are apparently, first, that it is usually present on the normal nasal mucous membrane and very often on the normal conjunctiva, throat, external auditory canal, and urethra; second, that it is not virulent for guinea-pigs; and third, that when it is found in inflammatory exudates it is accompanied by various pyogenic bacteria.²

The literature of otitis media shows clearly the influence of this theory. The bacteriology of this disease has been thoroughly studied and the pseudodiphtheria bacillus is frequently mentioned as occurring in the pus from such cases; but almost invariably it is treated as unimportant and of no causative significance. Many otologists do

* Received for publication April 6, 1907.

¹ A full bibliography of this subject is given by Schabad, *Jarhb. f. Kinderheilk.*, 1901, 54, p. 381; Lewandowsky, *Centralbl. f. Bakt.*, 1904, 36, p. 339; Graham-Smith, *Jour. Hyg.*, 1904, 4, p. 258.

² There are a few exceptions to the majority. Thus Bergey attributes pathogenic properties to the pseudodiphtheria bacillus, which he found in 43 per cent of 30 specimens of pus examined (*Univ. of Penn. Med. Bull.*, September, 1905, p. 198). Kruse and Pasquale, Goldcheider, Leber, Robertson, McRae and Jeffery, Johnston and Goodall, and Howard, all believe that it is concerned in certain inflammatory processes.

not even mention it.¹ Yet when one examines the reasons for the belief that the pseudodiphtheria bacillus is always a harmless saprophyte they seem open to question. The wide distribution of these bacilli, their occurrence in normal ears, throats, noses, etc., is not an argument against their pathogenic character, for it would apply equally well to the streptococcus, the pneumococcus, and the staphylococcus albus. As to virulence for guinea-pigs, there have been many strains reported which were more or less virulent.² Nor can it be shown that the pseudodiphtheria bacillus when present in the pus of otitis media has no part in the inflammatory process. On the contrary there is evidence to show that it is in some cases the real cause of the disease. Thus Warnecke³ found a non-virulent diphtheria-like bacillus in three cases of otitis media, once in pure culture. The first case was complicated with a progressive phlegmonous inflammation, the second with inflammation of the wound after an antrum operation, the third with meningitis and metastatic abscesses, and in all three cases the secondary lesions also contained the "xerosis" bacillus. L. D. Davis⁴ isolated from 12 cases of scarlatinal otitis media a diphtheria-like bacillus, virulent but non-toxic, which she regarded as the cause of the suppuration. Egerton Williams⁵ found diphtheria-like bacilli in 8 out of 62 cases of scarlatinal otitis media, and Duncan Forges⁶ found them in 32 out of 40 cultures from similar cases. Both think the organisms attenuated varieties of diphtheria bacilli, but Graham-Smith, on the ground of his examination of the ear discharges of 10 scarlet fever patients, concludes that these non-purulent organisms described by Forbes and Williams were not diphtheria bacilli but only related forms, diphtheria-like.

As a result of the study of various forms of suppuration, especially suppurative otitis media, I have been led to the belief that certain varieties of pseudodiphtheria bacilli play a much more important part in such processes than is generally credited to them. The

¹ A good summary of the literature of this subject is found in Süpfle's articles, *Centralbl. f. Bakt.*, Abtheil I, 1906, Orig., 42, p. 304.

² See discussion of virulence in *Jour. Infect. Dis.*, 1904, 1, p. 690.

³ *Munch. med. Wchnschr.*, 1900, 47, p. 1412.

⁴ *Proc. New York Path. Soc.*, 1898, p. 170.

⁵ *Brit. Med. Jour.*, 1901, 2, p. 1799.

⁶ *Jour. of Path. and Bact.*, 1903, 8, p. 448.

material studied consisted of 52 cases of suppuration in various parts of the body, and 142 cases of purulent otitis media. The miscellaneous suppurations were almost equally divided between chronic and acute cases, and included abscesses, infected wounds, ulcers, osteomyelitis, three cases of purulent conjunctivitis, and three of pyorrhea alveolaris. The pseudodiphtheria bacillus was found in 11 cases, 21 per cent of all. In four of them it was in pure culture. The 142 cases of otitis media yielded a still larger proportion, for 35 per cent of these cases showed pseudodiphtheria bacilli as the predominating organism. The difference between these two groups of cases disappeared, however, when the post-scarlatinal ear cases were tabulated separately, for then it was shown that the large majority of pseudodiphtheria cases came under this head.

The following table gives the percentage of cases in which this bacillus was either the only or the most important bacterium found:

TABLE 1.

	No. of Cases	No. with Pseudodiphtheria Bacilli	Percentage with Pseudodiphtheria Bacilli
Acute scarlatinal otitis media.	43	31	72%
Chronic scarlatinal otitis media.	9	5	55
Acute non-scarlatinal otitis media.	19	4*	21
Chronic non-scarlatinal otitis media.	71	11	15
Miscellaneous suppurations.	52	11	21

* 1 meningitis, 1 influenza, 2 measles.

It seems impossible that the difference between the acute scarlatinal and the acute non-scarlatinal should be accidental. The number of pseudodiphtheria cases in chronic otitis is not so great as in acute, but the same proportion obtains between scarlatinal and non-scarlatinal chronic otitis as between scarlatinal and non-scarlatinal acute otitis. The pseudodiphtheria cases are more than three times as numerous in the post-scarlatinal class as in the non-scarlatinal. All the cases included in this list as yielding pseudodiphtheria bacilli contained these bacilli as the predominating organism. Those in which only a few were found were ruled out as doubtful. In 9 of the acute scarlatinal cases this bacillus was found in pure culture, in 16 more there were only a few colonies of other organisms. Two of the chronic cases were complicated with mastoiditis and the pseudodiphtheria bacillus was recovered in pure culture from the mastoid

wound as well as from the ears. In another case there was a profuse conjunctivitis and the pseudodiphtheria bacillus was found in the discharge from the eye as well as in that from the ear. If the pseudodiphtheria bacillus has no pathogenic character, if it is simply a normal inhabitant of the auditory canal, there is no way of explaining why it should be found so frequently in scarlatinal otitis media. In nine of the 43 cases it was found in pure culture, that is, in over 20 per cent.

The belief that these bacilli are actively concerned in otitis media, especially in scarlet fever, was strengthened by the study of two small ward epidemics in the department for contagious diseases of the Cook County Hospital. In one of them, all four children who developed this complication and in the other all five children, showed pseudodiphtheria bacilli in large numbers in the pus from the ear. The ward with the five cases was small and crowded and contained at different times eight children, five of whom had suppurative middle-ear disease. The first one, a profuse double suppurative otorrhea with pseudodiphtheria bacillus in the pus, was followed after four days by two others, in both of which this bacillus was the predominating organism. While these three children were still in this ward two fresh cases of scarlet fever were brought in, both of whom, after seven and eight days, developed suppurative otitis media with pseudodiphtheria bacilli, one case yielding a pure culture. The other organisms found in four of these cases were, twice the staphylococcus albus, once the streptococcus, and once, both of these. Not only were these last present in small numbers, but no one organism was found in all of the five cases except the pseudodiphtheria bacillus.

The 51 strains isolated from the cases of otitis media and six of those isolated from suppurative lesions elsewhere (the others were not studied in detail) fall into two clearly defined groups which correspond to the types described, more or less fully, by many observers, as pseudodiphtheria and xerosis bacilli or, more recently, as pseudodiphtheria and diphtheria-like or diphtheroid. They are quite distinct from the virulent bacillus, usually called the "Ruediger bacillus,"¹ being distinguished from it not only by fermentation tests,

¹ *Jour. Infect. Dis.*, 1904, 1, p. 690.

but by the action of specific bacteriolytic, agglutinative, and opsonic sera.

Group 1, to which 40 strains belong, consists of short rods, rarely granular or barred, which may or may not decolorize by Gram, growing abundantly on agar, forming a cloudy growth in broth, in short corresponding to the pseudodiphtheria bacillus as usually described. The typical Hofmann bacillus however is usually said to form no acid or a very slight amount of acid in sugar broth and to be devoid of virulence for guinea-pigs.¹ With Hiss' serum-water medium all of the strains of this group which were tested—35 in all—fermented dextrose and saccharose, and failed to ferment maltose, lactose and dextrin. As to virulence for guinea-pigs, the majority were not virulent, but three out of 12 strains when injected intraperitoneally produced a general invasion of the body and death in 24–48 hours. Diphtheria antitoxin did not protect against a lethal dose.

Group 2 resembles the Klebs-Löffler bacillus very closely. These are long-barred or granular bacilli, often clubbed, staining by Gram, growing rather scantily on agar, more abundantly on blood serum, and fermenting in Hiss' serum-water medium, dextrose, and maltose always, dextrin in 60 per cent of the strains tested, and lactose in 10 per cent. Saccharose was never fermented by this group. They are more often virulent than Group 1. Four of the seven strains tested killed guinea-pigs, but one of these strains, otherwise indistinguishable from the others, was by this test shown to be *B. diphtheriae* for diphtheria antitoxin served to protect against it. It is evident that there is no hard and fast line between this group and the true Klebs-Löffler bacillus, and when the organisms are non-virulent it is absolutely impossible to separate the two.

Eleven cases of ear suppuration yielded bacilli of this type, six alone, five in conjunction with a bacillus of Type 1. Although the two types found in my cases are quite distinct and remain so after long cultivation, they are apparently equally pathogenic for human beings and capable of producing the same clinical symptoms.

It is often suggested that the human tissue upon which the organism finds lodgment may modify the character of the latter, and that

¹ See Graham Smith, *Jour. Hyg.*, 1906, 6, p. 286; Knapp, *Jour. Med. Res.*, 1904, 12, p. 475.

the same organism may appear as short and solid rods in one throat or ear and as long and diphtheria-like rods in another. In the ward epidemic described above, the first case had only diphtheria-like bacilli, the second, third, and fourth had the short, solid variety, and the fifth had both; yet in these cases the infection apparently was carried from the first case to the others. A. P. Ohlmacher¹ has stated that a bacillus of the pseudodiphtheria type may change to a diphtheria-like bacillus when passed through the body of the susceptible guinea-pig, and that, conversely, a long, slender, barred bacillus may change to the short, solid form after passage through an insusceptible animal, such as the white mouse. In this way Spirig² explained the different varieties of *B. diphtheriae* found in different throats in a house epidemic where the source of infection for all cases was the same.

That the two varieties found in my cases of otitis media are distinct, though closely related, is shown by their response to the action of specific immune sera. The serum of a rabbit immunized against one type is bacteriolytic for that type and not for the other. Rabbits were immunized by repeated injections of a typical member of Group 1 and the serum tested on 14 members of this group and 6 of Group 2. At the same time the serum of rabbits immunized against the "Ruediger bacillus" was tested on the same organism. The serum of the rabbits immunized against a strain of Group 1 was bacteriolytic for and agglutinated 13 other strains of this same group, but the serum of the rabbits immunized against the "Ruediger bacillus" had no more effect upon them than normal rabbit serum. On the other hand the serum bacteriolytic for Group 1 had no effect upon the "Ruediger bacillus." Neither serum had any effect upon six strains of Group 2; indeed the bacilli grew more abundantly in the tubes with serum than in the controls. It has not been possible as yet to procure a serum bacteriolytic for Group 2, because rabbits have apparently little resistance to these bacilli and invariably emaciate and die. These tests serve to separate three varieties of the large, loosely defined family of bacteria known as the pseudodiphtheria bacillus into distinct though closely related groups.

¹ *Jour. Med. Res.*, 1906, 7, p. 128.

² *Spirig, Ztschr. f. Hyg.*, 1899, 30, p. 511.

SUMMARY.

Two varieties of pseudodiphtheria bacilli are found frequently in suppurative processes, especially in the pus of post-scarlatinal otitis media. In this disease they are found so frequently as to render it probable that they play an important part in its causation. No less than 72 per cent of 43 cases of acute scarlatinal otitis media gave cultures of these bacilli and 20 per cent gave pure culture. Only 21 per cent of the cases of acute non-scarlatinal otitis gave the same bacilli.

These bacilli fall into two groups. Group 1 ferments saccharose but not maltose, is seldom virulent for guinea-pigs, and is agglutinated and killed by the serum of rabbits immunized against one member of the group. Group 2 ferments maltose but not saccharose, is more often virulent for guinea-pigs, and is not affected by the serum of rabbits immunized against Group 1. Neither group is affected by an immune serum which is bacteriolytic and agglutinative for the "Ruediger bacillus."

The belief that these bacilli may cause suppurative otitis is greatly strengthened by the fact, as I show elsewhere,¹ that the opsonic index of the patients for these bacilli has been found to undergo marked variations, and by the further observation that the injection of corresponding vaccines appears to modify definitely the course of the infection.

¹ P. 313.